SENSORY NEUROPATHY AFFECTS 40% OF HIV+ SOUTH AFRICANS DESPITE SAFER TREATMENTS AND 46% OF RISK IN THIS GROUP CAN BE PREDICTED BY ONE GENOTYPE PLUS DEMOGRAPHIC FACTORS!

Gaff J[1], Pillay P[2], Mbenda GN[2], Laws SM[1,3], Cherry C[2,4,5], Kamerman P[1,2], Price P[1,2].

[1] School of Pharmacy and Biomedical Science, Curtin University, Bentley, Australia
[2] School of Physiology, University of the Witwatersrand, Johannesburg, South Africa
[3] Collaborative Genomics Group, School of Medical and Health Sciences, Edith Cowan University, Joondalup, Australia
[4] Department of Infectious Diseases, Alfred Health and Monash University, Melbourne, Australia
[5] Burnet Institute, Melbourne, Australia

Background: HIV-associated sensory neuropathy (HIV-SN) is a small fibre neuropathy seen in 60% of South African HIV+ patients treated with stavudine. We established age, height and polymorphisms in adjacent genes - *P2X7R*, *P2X4R* and *CAMKK2* - as markers of susceptibility of HIV-SN in South African HIV+ patients receiving stavudine (model $p<0.0001$, $n=143$, Pseudo $R^2=0.19$).
Stavudine has now been phased out worldwide. The incidence of HIV-SN decreased from 34 to 14% in Jakarta, Indonesia. Susceptibility was then most clearly linked to lower CD4 T-cell counts, persistent HIV replication and three SNP in *CAMKK2*. Here we address whether the incidence of HIV-SN and its risk factors remain the same in South African patients treated without stavudine.

Methods: 75 HIV+ patients with African ancestry were recruited at clinics in Johannesburg as they commenced HIV treatment. Patients were assessed for neuropathy and thorough clinical details recorded at an initial visit and at follow-up appointments at 2, 4 and 6 months. Patients were genotyped for polymorphisms in the genes *P2X7R*, *P2X4R*, *CAMKK2* and *ANAPC5*.

Results: 29 of the 75 patients (38.7%) developed HIV-SN with 9/29 (12%) diagnosed prior to commencing HIV treatment. Two *P2X7R*, one *P2X4R*, four *CAMKK2* and one *ANAPC5* SNP associated with HIV-SN in bivariate analyses. The optimal logistic regression model predicting HIV-SN included one *P2X7R* and three *CAMKK2* SNP independently associated with HIV-SN after correcting for greater weight, lower CD4 T-cell count and a history of tuberculosis (model $p<0.0001$, $n=69$, pseudo $R^2=0.457$). This model explains a staggering **45.7%** of the risk of HIV-SN in this group.

Conclusion: Our findings confirm a role for *CAMKK2* in HIV-SN independent of stavudine and ethnicity. We are now evaluating whether the effects of *CAMKK2* extend to the brain by assessing neurocognitive loss in Indonesian HIV+ patients treated without stavudine.

Disclosure of Interest Statement: The authors have no conflicts of interest to declare